Zeitschrift für
Gastroenterologie
German Journal of Gastroenterology

2014 • 52. Jahrgang
www.thieme-connect.de/ejournals

Reprint

Position Paper of Scientific Societies for Recommended Usage of Endoscopic Biliodigestive Diversion in Germany – DDG/DGAV/DGVS

E. Siegel, G. Kähler, W. Schepp

ISSN 0044-2771

Thieme

Position Paper of Scientific Societies for Recommended Usage of Endoscopic Biliodigestive Diversion[1] in Germany – DDG/DGAV/DGVS

Authors E. Siegel[1], G. Kähler[2], W. Schepp[3]

Affiliations Affiliation addresses are listed at the end of the article.

Bibliography
DOI http://dx.doi.org/10.1055/s-0034-1385177
Z Gastroenterol 2014; 52: 1–7

ISSN 0044-2771

Correspondence
Prof. Dr.Wolfgang Schepp
Clinic for Gastroenterology, Hepatology and gastroenterologic oncology, Bogenhausen Clinic, Städtisches Klinikum München GmbH
Englschalkinger Straße 77
81925 München
Tel.: Tel.:++49/89/92 70 20 60
Fax: Fax:++49/89/92 70 24 86
Gastroenterologie.kb@klinikum-muenchen.de

Introduction

Type 2 diabetes mellitus is a frequently occurring metabolic disease. In the last 15 years the prevalence has shown a further marked increase in Germany and is now 7.2 % for adults between 18 and 79 years of age (women: 7.4 %, men: 7 %). Men and women with obesity make up a sub-group with an especially pronounced risk of illness [8]. The prevalence of overweight (BMI = 25 kg/m) has stagnated for years at a high level; among 18 through 79 year olds, 67.1 % of men and 53 % of women are overweight. The prevalence of obesity, which is characterized by a BMI ≥ 30 kg/m, has increased significantly. Currently 23.3 % of men and 23.9 % of women are obese and the rate is rising in young adults, in particular [10].

Patients with type 2 diabetes mellitus – DMT2 -, above all many of these in early stages, can effectively control their blood sugar through diet, weight reduction, and physical activity. In case these measures for effective control are not sufficient, oral and/or injectable medications are administered as a rule. In spite of diet and/or pharmacological therapy, many patients do not manage to maintain their individual therapeutic goal (HbA1c-target range: 6.5 – 7.5 %) in accordance with the National Disease Guideline for therapy of type 2 diabetes – NVL DMT2 – (August 2013 – AWMF- Register No.: nvl-001 g). Patient compliance in a prescribed therapy program is one of the main, limiting factors for controlling blood sugar through orally administered or injectable agents. The increasing complexity of the medical treatment program of the patient has a negative effect on compliance. This complexity, in combination with the necessary treatment of concomitant diseases such as e. g. high blood pressure and hyperlipidemia, is an increasing challenge for patients.

Treatment by means of endoscopic biliodigestive diversion (DJBS) – EndoBarrier®, GI Dynamics Inc., Lexington, MA, USA – also synthetic conduit or endoscopic bypass tube – is a new, innovative therapeutic approach for obese diabetes patients.

The opportunity is used to influence the diabetic metabolic condition via a small intestine bypass. In the process, food and digestive secretions do not come into contact in the duodenum, but are instead transported approx. 60 cm in parallel through the jejunum – separately through the endoscopically inserted synthetic conduit.

The thus distally displaced digestion not only effects a significant weight reduction, but rather above all influences the glucose metabolism quite favorably. Similar effects are known from operative bypass procedures and therapy with GLP-1 analogs and are based primarily on hormonal regulation effects. The endoscopic and temporarily implantable duodenojejunal synthetic conduit is characterized by minimal invasiveness, good tolerance and complete reversibility. For obese diabetes patients, DJBS thus represents a new, additional therapy option which with respect to the combination of effectiveness and invasiveness up to now has been without comparable alternatives.

Status quo of the endoscopic biliodigestive diversion

Endoscopic biliodigestive diversion (DJBS) was first used within the scope of studies in 2007 in the USA, the Netherlands, Chile and Brazil. Upon gaining CE certification for a 12 month use in October 2010, the procedure was clinically applied in specialized centers in Europa, including Germany, the Netherlands, Great Britain, Italy, Spain, the Czech Republic, Austria and Switzerland. In Germany, the DJBS was performed at the University Clinic Hamburg-Eppendorf for the first time

[1] Also: duodenal-jejunal bypass sleeve (DJBS)

in November 2010. Meanwhile 37 centers worldwide have added DJBS to their therapeutic spectrum. The faculties participating in the treatment vary from hospital to hospital. As a rule, patients undergo long-term treatment from a metabolic and diabetes center and given therapy. The endoscopic implementation of the treatment is carried out by internistic, endoscopic or surgical specialists. The anesthesiology and intensive care medicine is likewise part of the treatment, to be precise the anesthesia during the implantation/explantation and the subsequent monitoring, which frequently requires increased attention and additional treatment due to the obesity. The long-term post-operative care is usually back at Endocrinology (Diabetology) with its multidimensional diabetes therapy through metabolic or diabetes centers that can successfully implement this multi-disciplinary treatment approach and have a correspondingly high degree of specialization in the affected patient group. From an organizational standpoint, metabolic or diabetes centers can be physically separate from the implantation center; however this requires very close coordination when it comes to patient treatment. In this way the greatest possible safety is guaranteed for the patient and lasting success of the treatment is ensured. Prior to the introduction of the therapy at a new hospital, an intensive training on the part of the manufacturer takes place. In this context, physicians experienced in the therapy come to the selected hospitals in order to share their knowledge right away. The manufacturer supports the application within the scope of multidisciplinary treatment concepts in specialized centers.

Indication and alternative therapeutic methods

The National Disease Guideline for the therapy of type 2 diabetes (August 2013 – AWMF-Register No.: nvl-001 g) provides various therapeutic algorithms for the treatment of type 2 diabetes, which in the further progression of the disease results in a long-term therapy with insulin. The indication for the application of DJBS should take place in specialized metabolic or diabetes centers which have the necessary experience in patient selection and have undergone intensive training with respect to the application of this new method of treatment. For the purpose of clarification of a comprehensive case history and for diagnosis the specialized metabolic or diabetic centers should have an interdisciplinary treatment team (endocrinology/psychosomatic/nutritional medicine). This interdisciplinary treatment team can be made up of both specialists from the hospital as well as from the private practice sector and requires a good collegial, cooperative collaboration.

The post-operative care necessary during and after the DJBS should likewise take place via the aforementioned metabolic or diabetes centers. The DJBS is authorized for the treatment of adult patients (minimum age: 18 years) with type 2 diabetes mellitus and overweight. Due to the present evidence and ongoing studies, whose current interim results imply that the previous results are proven to be true, the DJBS is medically indicated for obese diabetes patients (type 2 diabetes + BMI 25 – 45 – alternative BMI 30 – 45) who using a pharmaceutical double combination or with (increased) insulin dosage are not able to reach their personal therapeutic goal over a period of 3 – 6 months (National Disease Guideline for the Therapy of type 2 diabetes (August 2013 – AWMF-Register No.:nvl-001 g). Conventional therapy options are exhausted for this group of patients and thus the DJBS represents a genuine therapy option and supplement for this patient clientele. In addition, the use of DJBS seems medically advisable when a bariatric surgery is medically indicated, but due to an increased operative risk a preoperative weight reduction (stage concept/“bridging”) is clinically necessary for preparation for such an operation (S3 guideline: Surgery of obesity: DGAV CA-ADIP; June 2010).

Contraindications are primarily prior operations on the stomach and duodenum, chronic ulcera duodenal as well as biliary tract diseases requiring access to the papilla vateri. In addition, the necessity of an ingestion of acetylsalicylic acid (ASA) or non-steroidal anti-inflammatory drugs (NSAIDs) as well as an existing or planned pregnancy constitute contraindications. Various bariatric surgical techniques are available for patients for whom the treatment of obesity is medically indicated. The procedure that best corresponds to DJBS in the mechanism of action is the biliopancreatic diversion or the gastric bypass. This is a very invasive operative therapy that performs complex and lasting changes to the anatomy of the digestive tract.

Description of endoscopic biliodigestive diversion

The DJBS is an innovative procedure for non-operative and drug-free therapy of patients with type 2 diabetes mellitus and obesity, in which a duodenojejunal synthetic conduit (also: bypass tube) is endoscopically introduced. In the following the therapy is explained in detail.

Main elements

For the endoscopic implantation or explantation of the synthetic conduit (bypass tube), a set is made available which contains all the necessary components. All of these components are provided for single use only.

- Synthetic conduit (mixture of expanded polytetrafluorethylene ePTFE and fluoroethylenepropylene PEP) with anchoring system at the proximal end (made of Nitinol)
- Coaxial catheter with tension wire in the inside portion
- Capsule in which the synthetic conduit is compressed with anchor ring on the distal end of the outside portion of the coaxial catheter
- Several functional grips for feeding of the conduit, removal of the anchor ring etc. on the proximal end of the catheter
- Catheter with retrieval hooks and protective device for tissue-conserving removal of the synthetic conduit

Application

For treatment by means of DJBS, after indication the patient is admitted to the hospital in a specialized metabolic or diabetes center. An endotracheal anesthesia provides the greatest possible safety and radius of operation for a rapid and successful implantation of the synthetic conduit. The procedure is performed as a 4-hand procedure. First of all (preferably in left lateral position), the gastroscope is inserted. In the next step, a guide wire is fed up to the duodenum. The synthetic conduit with its anchor ring is in a narrow capsule that is fed via the guide wire up to the pylorus. The correct position of the capsule is ensured with the assistance of gastroscopic visual inspection and fluoroscopy.

Now with the help of the tension wire the approx. 60 cm long, an opaque tube made of fluoropolymer is unfolded from the capsule into the jejunum. On the tip is a “guide ball” which, after successful unfolding of the tube via a manual mechanism via catheter is separated and eliminated from the body naturally. The complete unfolding of the conduit is inspected via fluoroscopy. Afterwards,

the anchor ring made of Nitinol is removed, which independently unfolds in the bulbus duodeni and anchors the synthetic conduit on the intestinal wall.
Finally the location of the conduit is inspected via fluoroscopy with X-ray contrast medium as well as optically assessed after removal of the empty capsule with the gastroscope.

Post-operative Care

After the implantation, a monitoring in the recovery room or in intensive care is often necessary to a far greater extent than normal, since obese patients are especially subject to the danger of respiratory depression/apnea.
The duration of the entire in-patient treatment is 3 – 4 days as a rule. Due to the hormonal changes which have a massive influence on the metabolism, in particular the initial effects on the glucose metabolism must be closely monitored and the medication adjusted to the said effects. Moreover, in the first few days after implantation there can be symptoms (usually feelings of pressure or pain in the abdomen and/or digestive problems such as nausea, vomiting, diarrhea) which require an in-patient observation. Here in particular the frequently occurring mild and as a rule low-risk complications – e. g. pressure pain in the abdominal region, nausea, vomiting, loss of appetite – are to be distinguished from more serious complications, e. g. hemorrhaging or dislocations. As long as the synthetic conduit is in situ, the ingestion of 2 × 40 mg Omeprazol daily is necessary in order to minimize the risk of bleeding. The synthetic conduit itself does not require any special kind of diet. However, the patient should make certain that food is chopped into small pieces and drink lots of fluids. After 10 – 12 months the synthetic conduit is endoscopically removed in an approx. 2-day in-patient stay. For this purpose the retrieval catheter contained in the treatment set is used, which with the help of a cone protects the mucous membrane from injuries through the anchor ring when being removed.

Therapeutic effect

The therapeutic effect of the DJBS for patients with type 2 diabetes mellitus and obesity consists in a combination of a strong, normalizing effect on diverse metabolic parameters, in particular the glucose metabolism, and an additional significant weight reduction. The synthetic conduit prevents digestion from insertion in the duodenum. Only after a distance of approx. 60 cm is there a merging of food and digestive secretions in the course of the jejunum. The previously proven effects on the glucose metabolism include an improvement of the fasting blood sugar, glucose tolerance, the HbA1c value, fasting insulin, the postprandial glucagon and GLP-1 secretion and some other hormonal parameters (**Table 1**). These effects can be explained on the one hand by the “foregut” theory and on the other hand by the “hindgut” theory or a combination of the two [13].
Both theories describe the change of hormonal signals in the proximal or distal small intestine, which result from the fact that the food does not come into contact with the duodenum and the proximal jejunum, or (sometimes) undigested food reaches the distal jejunum.
In the case of the foregut theory it is assumed that in the event of a diabetic metabolic condition prevailing anti-incretin mechanism is switched off. The stimulation of the GLP-1 secretion in the distal ileum is on the other hand viewed as a mechanism of the hindgut theory. These theories are to be assessed as first indications of a presumably much more complex mechanism of action. Further studies are required for a complete understanding of the mechanism of action.
Additional elements of the therapeutic effect consist of weight loss and the improvement of cardio-vascular risk factors such as high blood pressure, hyperlipidemia or metabolic syndrome. Up to now it has not been possible to prove malabsorption.

Scientific Proof of Effectiveness

Meanwhile, since the first case report 2008 [12] a series of clinical studies of DJBS have been carried with a total of more than 300 patients. Previously, in 2006 – 2008 there were some animal experiment series on effectiveness and applicability of the therapy. These studies are listed in Appendix A. Since the DJBS was originally developed with the primary goal of weight reduction, the earlier studies focus primarily on weight-specific end points such as excess weight loss (EWL), BMI and total weight. Accompanying diseases associated with obesity such as high blood pressure, hyperlipidemia or type 2 diabetes mellitus were of secondary importance in the studies. Due to the strikingly pronounced and rapid improvement of the glucose
metabolism after implantation of the synthetic conduit, this topic quickly became the focus of subsequent studies. An attempt was made to show the mechanisms of action on the one hand and on the other hand to describe the effects more completely. Also the current recommendation directs our attention primarily on the treatment of type 2 diabetes mellitus.

Effects on glucose metabolism

The effects on glucose metabolism were investigated in the clinical studies listed in **Table 1**. Common to all of the studies is the early onset of the effect on the glucose metabolism and thus also (at least in parts) independence of weight loss [2]. The earliest measured time with normalization of the glucose metabolism parameters was at 24 hours after implantation [12]. In summary, the following changes can be noticed:

- Reduction of the fasting blood sugar
- Improvement of glucose tolerance
- Reduction of the HbA1c value
- Reduction of the fasting insulin
- Reduction of the postprandial glucagon secretion
- Increase of the postprandial GLP-1 secretion
- Reduction of HOMA-IR values
- Rise of the Matsuda index
- Improvement of insulin resistance
- Improvement of insulin sensitivity (increase adiponectin)
- Improvement of the blood sugar daily level
- Reduction of the AUC in postprandial glucose increase
- Dose reduction or discontinuation of existing diabetes medication

Concerning the description of the effects after explantation of the synthetic conduit, the results to hand are still insufficient in order to draw a clear conclusion. From Cohen et al. [2], it can be shown that one week after explantation of the synthetic conduit the GLP-1 secretion dropped again, while the reduction of the postprandial glucagon and glucose increase was preserved. In another study [5], the positive effects on the glucose metabolism slowly receded 2 weeks after explantation of the synthetic conduit. The reduction of the HbA1c values in comparison to the initial value was still unchanged 3 months after the explantation

Table 1 Clinical studies with investigation of glucose metabolism.

author (year)	country	study type	participants (n and further characteristics)	duration of treatment/study	effects on glucose metabolism	
Cohen et al. (2013)b	Brazil	prospective, single-center, open-label	16; diabetes, moderate obesity	52 weeks and 26 weeks after explantation	fasting blood sugar	reduction from 203.3 ± 13.5 to 155.1 ± 13.1 mg/dl, or 150.2 ± 10.06 mg/dl after explantation
					HbA1c	reduction from 8.6 ± 0.2 % to 7.5 ± 0.4 % or 7.8 ± 0.4 % after explantation
					HOMA-IR	reduction from 6.6 to 3.0 or 4.3 after explantation
					Matsuda Index	increase of 1.7 to 3.2 or 2.4 after explantation
					insulin parameter/ secretion	no significant change
					C-Peptide	no significant change, except reduction fasting C-Peptide 1 and 52 weeks after explantation
Cohen et al. (2013)a	Brazil	prospective, single-center, open-label	23; diabetes, moderate obesity 20 successful implantations; 4 terminations	52 weeks	fasting blood sugar	reduction from 207 ± 61 to 155 ± 52 mg/dl
					HbA1c	reduction from 8.7 ± 0.9 % to 7.5 ± 1.6 %
de Jonge et al. (2013)a	Netherlands	prospective, single-center, open-label	17; diabetes; severe obesity	24 weeks and 1 week after explantation	GLP-1	increase postprandial from 4.440 ± 249 to 6.008 ± 429 pmol/L/min; fasting GLP- 1 unchanged
					Glucagon	reduction postprandial from 23.762 ± 4.732 to 13.207 ± 1.946 pg/mL/min; fasting Glucagon unchanged
					total GIP	reduction postprandial from 115.272 ± 10.971 to 88.499 ± 10.971 pg/mL/min; fasting GIP unchanged
					fasting blood sugar	reduction from 11.6 ± 0.5 to 8.6 ± 0.5 mmol/l
					fasting insulin	no significant change
					HbA1c	reduction from 8.4 ± 0.2 % to 7.0 ± 0.2 %
					HOMA-IR	reduction from 14.6 ± 5.8 to 9.2 ± 3.5
de Moura et al. (2012)	Brazil	prospective, single-center, open-label	22; diabetes, severe obesity, 9 terminations, 15 at aleast. 24 weeks	52 weeks	fasting blood sugar	reduction by 37.1 ± 11.8 mg/dl
					fasting insulin	reduction by 10.1 ± 4.2 µU/ml
					HbA1c	reduction by 2.3 ± 0.3 %
Escalona et al. (2012)	Chile	prospective, single-center, open-label	42; severe obesity, 39 successful implantations, 15 terminations, 6 diabetes.	52 weeks and months 1, 3 and 6 after explanation	fasting blood sugar	reduction from 104 ± 6 to 94 (all) ± 6 mg/dl
					fasting insulin	reduction by 7.0 ± 1.6 µU/ml (non-diabetics)
					HbA1c	reduction by 1.4 ± 0.6 % (only diabetics)
					HOMA-IR (non-diabetics)	reduction by 1.7 ± 0.4
de Moura et al. (2011)	Brazil	prospective, single-center, open-label	81; diabetes; severe obesity, 75 successful implantations, 1 exclusion due to non-compliance, only 54 with insulin resistance, 16 terminations	6 months	HbA1c	reduction in all subgroups of the study, overall at 70.3 % values < 7 % after 6 months
					TG/HDL quotient (insulin resistance)	reduction from 5.75 to 4.36
Schouten et al. (2009)	Netherlands	randomized, prospective, single-center, open-label	30, severe obesity, 26 successful implantations, 8 terminations, 8 diabetes, 324 weeks, 11 control group (diet), 2 diabetes	12/24 weeks	fasting blood sugar	not significant reduction by 1.8 vs. 0.9 mmol/l (control group)
					HbA1c	not significant reduction by 1.1 % vs. 0.4 % (control group) not significant
Tarnoff et al. (2009)	Chile	randomized, prospective, single-center, open-label	26; severe obesity, 25 successful implantations, 5 terminations, 3 diabetes, 14 control group (diet), 1 diabetes	12/24/36 weeks and 4 weeks after explantation	diabetes medication	reduction of HbA1c or values held in therapeutic in spite of discontinuation or dose reduction

Table 1 (Continuation)

author (year)	country	study type	participants (n and further characteristics)	duration of treatment/study	effects on glucose metabolism	
Rodriguez et al. (2009)	Chile	randomized, prospective, single-center, open-label	12; diabetes, severe obesity, 3 terminations, 10 at least, 24 weeks; 6 control group (pseudo-implantation)	24/52 weeks	fasting blood sugar	reduction by 83 vs. increase by 16 mg/dl (control group)
					HbA1c	not significant stronger reduction vs. control group
					diabetes medication	40 % vs. 25 % without medication (control group)
Rodriguez et al. (2008)	Chile	prospective, single-center, open-label	12; severe obesity, 2 terminations, 4 diabetes	12 weeks	fasting blood sugar	normal over 12 weeks without medication
					HbA1c	lowered in 3 patients, 1 no change
					diabetes medication	discontinued

and had declined by 0.6 % 6 months after. An investigation 26 weeks after explantation showed that along with the weight, the values for HbA1c, glucose (fasting and postprandial), HOMA-IR and Matsuda index (for the insulin resistance/sensitivity) in comparison to the initial values had still significantly improved [1]. Recently it could be shown that DJBS is still effective in the case of moderate obesity [1, 2]. With this result the application is moving appreciably in the direction of an early use in the course of the diabetes disease, before other comorbidities of diabetes and obesity place too much stress on the patient.

Effects on other metabolic parameters

The weight reducing effect was also proven in further studies in addition to the studies listed in the table (see Appendix A). It lies in a range from average to minus 9.1 kg/m2 BMI or 47 % EWl [7]. Frequently a higher percentage of values above 10 % is achieved. In addition, some studies also show an improving effect on cardiovascular risk factors – among others high blood pressure and hyperlipidemia. Noteworthy in particular is a recently published study which investigates the effects of the DJBS on the non-alcoholic fatty liver disease (NAFLD) [3]. NAFLD occurs frequently in connection with type 2 diabetes mellitus and obesity and can lead to fatty liver cirrhosis and liver cell cancer in the terminal stage. The characteristic serum parameters were significantly improved through treatment with the duodenojejunal synthetic conduit. The positive effect was demonstrable in some cases 6 months after explantation.

Safety of the endoscopic biliodigestive diversion – complications/adverse effects

▼

The data compiled in the clinical studies on the safety of the application of the DJBS shows that the implantation can fail, the synthetic conduit if necessary must be removed prematurely or side effects may occur. The intervention itself is described as free of complications except for a case of chest pains due to a distension of the esophagus [15].

The failure of the implantation, which decreases with the learning curve of the practitioner, can be caused by anatomical circumstances. Usually a shortened bulbus duodeni is present, in which an anchoring of the synthetic conduit is not possible. In some cases after variable time periods there is a location change of the anchor ring or of the synthetic conduit. For one, it can migrate distally, secondly it can get caught in the plane of the lumen. Frequently this is accompanied by pain in the abdomen; however, sometimes patients have no symptoms. The side effects are described overall as mild to moderate. The most frequent side effects are: abdominal pain, nausea, vomiting and hemorrhaging. As a rule, their incidence is limited to the first 1 – 2 weeks after the implantation. More rarely the synthetic conduit has to be prematurely explanted due to enduring more pronounced side effects. There are also individual cases described of rarer complications such as e. g. cholecystitis [7]. The premature removal can also be necessary as a result of congestion of the synthetic conduit. As a rule, explantation of the synthetic conduit is sufficient for the successful treatment of the side effects. Locally, in the region of the anchoring there are signs of inflammation in the mucous membrane after the explantation, frequently accompanied by pseudo-polyps.

In a study from 2009 it was shown that the pylorus function remained undisturbed and in the event of a good presentability of the synthetic conduit in the x-ray it was possible to demonstrate the tightness [9]. After the product was due to the clinical experiences and in particular the anchoring mechanism was able to be improved, fewer complications are expected in the future, among others fewer dislocations and hemorrhages. In the available studies the application was consistently rated as safe, without serious side effects being expected.

Recommendation for application of biliodigestive diversion

▼

For obese patients with type 2 diabetes the DJBS represents a therapy option and supplement to conventional therapy corresponding to the National Disease Guideline for the therapy of type 2 diabetes (August 2013 – AWMF-Register No.: nvl-001 g). We recommend consideration of the DJBS as a therapy alternative for the treatment of adult patients (minimum age: 18 years) with type 2 diabetes mellitus and overweight (BMI 30 – 45) when these patients cannot reach their individual therapy goals over a period of 3 to 6 months under the therapy algorithm in accordance with the National Disease Guideline for the therapy of type 2 diabetes (August 2013 – AWMF-Register No.: nvl-001 g). Currently there is no other promising therapy option for this patient population.

For morbidly obese patients (BMI 45 -> 60) the use of endoscopic biliodigestive diversion is also medically advisable when a bariatric operation is medically indicated, but due to the increased opera-

tive risk for preparation for such an operation a preoperative weight reduction (stage concept/"bridging") is clinically necessary (S3-Guideline: Surgery of the obese; DGAV CA-ADIP; June 2010).

The therapeutic approach of the DJBS combines the pronounced positive effects on the metabolism, as is known from operative procedures (e. g. Roux-en Y), with a simple, safe and completely reversibly application. As a result, for the first time an effective therapy option is available for conservative insufficiently treatable obese type 2 diabetics. With the endoscopic biliodigestive diversion an effective treatment of diabetes mellitus and simultaneously a significant weight reduction is brought about, without the necessity of a surgical intervention with effects on the overall further existence of the patient. Building on the previous available studies currently RCTs in the Netherlands, France, Great Britain and the USA are in implementation with a total of 977 patients to be included. ▶ **Table 2**. The considered time period should be an entire year in all studies. Older studies have predominantly used a prototype of the available product which was not commercially used (no CE certificate). Therefore these studies only consider a time period of 12 or 24 weeks. In the light of increasing prevalences for type 2 diabetes mellitus and obesity, the group of patients who are suitable for endoscopic biliodigestive diversion is set to increase. From the viewpoint of the undersigned scientific societies therefore, the expansion of the treatment spectrum is of the greatest importance. Both type 2 D diabetes mellitus and also obesity are chronic diseases which are accompanied by a great number of comorbidities, thus making a successful treatment all the more difficult, the more advanced the disease is. In addition, the many years of treatment of this multiple morbid patient group represents an immense cost factor in health care. In addition one must consider the economic costs of the victim's loss of production.

The experiences gathered thus far in Germany clearly show good practicability and tolerance on the basis of feedback from individuals.The trained physicians are quite satisfied with the application and regularly report successful implantations. The affected patients are grateful for this new treatment option which can significantly change the perspective of the progression of the disease. The specialized treatment method of the endoscopic biliodigestive diversion is suitable exclusively for use in selected centers which, for one thing have completed training under the supervision of specialists and for another can ensure the correct diagnosis and long-term treatment success through a multidisciplinary treatment approach. In the process the metabolism or diabetes center (indication + aftercare) can be physically separate from the implantation center. In this connection however, care must be taken that there is a very good collegial cooperation and coordination.

It is intended that the treatment data of the patients gathered during and after DJBS within the scope of the "EndoBarrier-Register" that was conducted at the University Clinic Hamburg-Eppendorf under the direction of Dr. med. Aberle be subject to the approval of the patients. As a result important clinical real-life data are collected and merged in structured manner and can be subsequently evaluated. This prospective data then results in the fact that – in addition to the studies listed in ▶ **Table 2** that are currently being implemented – the evidence for DJBS improves over the course of time.

Table 2 Clinical studies currently in the planning stages or being implemented.

study identifer	time	study type	n	intervention	comparator	patient population	endpoints	remarks
NCT01 728 116	December 2012 to June 2015	multi-center RCT	500 333/167	duodenal-jejunal bypass liner (DJBS)	sham procedure	type 2 DM in obese subjects	HbA_{1c} weight reduction reduction of cardiovascular risk factors	
NCT00 985 114	completed in 2013 publication expected in 2014	multi-center RCT	71 34/37	duodenal-jejunal bypass liner (DJBS)	life-style changes + diet	type 2 DM and obesity	HbA_{1c} reduction in diabetic medication weight reduction	
ENDOMETAB french STIC study	January 2014 to March 2017	multi-center RCT	174 116/58	duodenal-jejunal bypass liner (DJBS)	conventional treatment	metabolic syndrome subjects	reduction in rates of metabolic syndrome weight reduction improvement in cardiovascular risk factors QOL (SF36 & IWQOL) Cost benefit	EC approval pending independent study – financed by French MoH
UK EME MRC study	January 2014 to January 2017	multi-center RCT	160 80/80	duodenal-jejunal bypass liner (DJBS)	conventional treatment	type 2 DM in obese subjects	significant improvement in metabolic state (IDF) Weight reduction	independent study – financed by EME MRC grant
ABCD study	July 2013 to October 2016	multi-center RCT	72 24/24/24	duodenal-jejunal bypass liner (DJBS)	medical treatment – Liraglutide, 1.8 mg – DJBS w/o Liraglutide – DJBS + 1.2 mg Liraglutide	type 2 DM in obese subjects	HbA_{1c} Weight reduction	independent study – financed by ABCD grant

Affiliations

[1] Department of Internal Medicine – Gastroenterology, diabetology and nutritional medicine, St. Josefskrankhaus, Heidelberg (for the German Diabetes Society)
[2] Central Interdisciplinary Endoscopy, Mannheim, University Medicine Mannheim, (for the German Society for General and Visceral Surgery)
[3] Clinic for Gastroenterology, Hepatology and gastroenterologic oncology, Bogenhausen Clinic, Städtisches Klinikum München GmbH, Munich (for the German Society for Digestive and Metabolic Diseases)

References

1 *Cohen R*, *le-Roux CW*, *Papamargaritis D et al.* Role of proximal gut exclusion from food on glucose homeostasis in patients with Type 2 diabetes. Diabet Med 2013; 30: 1482 – 1486
2 *Cohen RV*, *Neto MG*, *Correa JL et al.* A pilot study of the duodenaljejunal bypass liner in low body mass index type 2 diabetes. J Clin Endocrinol Metab 2013; 98: E279 – E282
3 *De Jonge C*, *Rensen SS*, *Koek GH et al.* Endoscopic Duodenal-Jejunal Bypass Liner Rapidly Improves Plasma Parameters of Nonalcoholic Fatty Liver Disease. Clin Gastroenterol Hepatol 2013; 11: 1517 – 1520
4 *De Jonge C*, *Rensen SS*, *Verdam FJ et al.* Endoscopic DuodenalJejunal Bypass Liner Rapidly Improves Type 2 Diabetes. Obes Surg 2013: 1354 – 1360
5 *De Moura EGH*, *Martins BC*, *Lopes GS et al.* Metabolic improvements in obese type 2 diabetes subjects implanted for 1 year with an oscopically deployed duodenal-jejunal bypass liner. Diabetes technology & therapeutics 2012; 14 (2): 183 – 189. DOI: 10.1089/dia.2011.0152
6 *De Moura EGH*, *Orso IRB*, *Martins BDC et al.* Improvement of insulin resistance and reduction of cardiovascular risk among obese patients h type 2 diabetes with the duodenojejunal bypass liner. Obesity surgery 2011; 21 (7): 941 – 947. DOI: 10.1007/s11695-011-0387-0
7 *Escalona A*, *Pimentel F*, *Sharp A et al.* Weight loss and metabolic improvement in morbidly obese subjects implanted for 1 year with an oscopic duodenal-jejunal bypass liner. Annals of surgery 2012; 255 (6): 1080 – 1085. DOI: 10.1097/SLA.0b013e31825498c4
8 *Heidemann C*, *Du Y*, *Schubert I et al.* Prevalence and development of known diabetes mellitus. Results of the study on the health of adults in Germany (DEGS1). Federal Health Gazette, Health Research, Health Protection 2013; 56 (5): 668 – 677 Retrieved from http://edoc.rki.de/oa/articles/reStimZmeS2/PDF/28z6BcQzEazE.pdf
9 *Levine A*, *Ramos A*, *Escalona A et al.* Radiographic appearance of endoscopic duodenal-jejunal bypass liner for treatment of obesity and type 2 diabetes. Surgery for obesity and related diseases 2009; 5 (3): 371 – 374
10 *Mensink GBM*, *Schienkiewitz A*, *Haftenberger M et al.* Overweight and obesity in Germany. Results of the study on the health of adults in Germany (DEGS1). Federal Health Gazette, Health Research, Health Protection 2013; 56 (5): 786 – 794. DOI: 10.1007/s00103-012-1656-3
11 *Rodriguez L*, *Reyes E*, *Fagalde P et al.* Pilot clinical study of an endoscopic, removable duodenal-jejunal bypass liner for the treatment of type 2 diabetes. Diabetes technology & therapeutics 2009; 11 (11): 725 – 732. DOI: 10.1089/dia.2009.0063
12 *Rodriguez-Grunert L*, *Galvao Neto MP*, *Alamo M et al.* First human experience with endoscopically delivered and retrieved duodenal-jejunal bypass sleeve. Surgery for obesity and related diseases: official journal of the American Society for Bariatric Surgery 2008; 4 (1): 55 – 59. DOI: 10.1016/j.soard.2007.07.012
13 *Romero-Talamás H*, *Brethauer SA*. A novel approach for diabetes: recent evidence on endoluminal liners. Diabetes Management 2013; 3 (3): 235 – 244
14 *Schouten R*, *Rijs CS*, *Bouvy ND et al.* A multicenter, randomized efficacy study of the EndoBarrier Gastrointestinal Liner for presurgical weight loss prior to bariatric surgery. Annals of surgery 2010; 251 (2): 236 – 243. DOI: 10.1097/SLA.0b013e3181bdfbff
15 *Tarnoff M*, *Rodriguez L*, *Escalona A et al.* Open label, prospective, randomized controlled trial of an endoscopic duodenal-jejunal bypass sleeve versus low calorie diet for pre-operative weight loss in bariatric surgery. Surgical endoscopy 2009; 23 (3): 650 – 656. DOI: 10.1007/s00464-008-0125-4